



A Junctional Rhythm Caused by Administration of Intravenous Phenytoin

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ABSTRACT

Introduction: We present the case of a patient with symptomatic junctional rhythm caused by administration of intravenous phenytoin. However, bradycardia and hypotension are more commonly associated with rapid infusion of intravenous phenytoin. In our patient, the rate of intravenous phenytoin administration was <50 mg/min.

Case Report: A 79-year-old woman presented to the emergency department with altered mental status for 2 h and focal seizure. After phenytoin was intravenously infused over 45 min, junctional rhythm, unresponsiveness, and hypotension developed. Atropine, dopamine, and transcutaneous pacing were initiated. After the intervention, a normal sinus rhythm with a normal heart rate was maintained. The patient was admitted to the neurological intensive care unit.

Conclusion: Emergency physicians should monitor patients for possible arrhythmic effects of intravenous phenytoin therapy. In addition to geriatric patients and patients with a history of cardiac disease, there may be an increased risk of cardiotoxicity for phenytoin even at the recommended dose and infusion rate in patients with end-stage renal disease.

Keywords: Bradyarrhythmias, phenytoin, cardiotoxicity

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Introduction

Phenytoin is an anticonvulsant drug used for treating many seizure disorders. It is also a class IB anti-arrhythmic agent, although it is now infrequently used for that indication. Rapid administration of intravenous phenytoin can cause hypotension, bradyarrhythmias, and occasional asystole (1, 2). In this case report, we aimed to validate that phenytoin can cause cardiotoxicity even at the recommended dose and infusion.

Case Report

A 79-year-old woman presented to the emergency department with an altered mental status for 2 h and focal seizure (tonic-clonic movement of the right upper limb). Her medical history included end-stage renal disease for which she was on hemodialysis, type 2 diabetes mellitus, hypertension, coronary artery disease, and a history of brain tumor surgery. Her home medications included levetiracetam, clopidogrel, carvedilol, and gabapentin.

The patient's weight was 68 kg, and her vital signs on admission were a temperature of 36.6°C, blood pressure of 150/71 mm/Hg, heart rate of 117 beats/min, and respiratory rate of 20 breaths/min, and her oxygen saturation was 91% while breathing room air. Her Glasgow Coma Scale was 12, and she appeared apathetic. The remaining physical examination results were normal. Laboratory findings on admission were hemoglobin level of 8 g/dL, serum sodium level of 137 meq/L, potassium level of 5.34 meq/L, glucose level of 112 mg/dL, creatinine level of 9.29 mg/dL, and urea level of 162.7 mg/dL. On blood gas analysis, the pH

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FIGURE 1. ECG showed a normal sinus rhythm

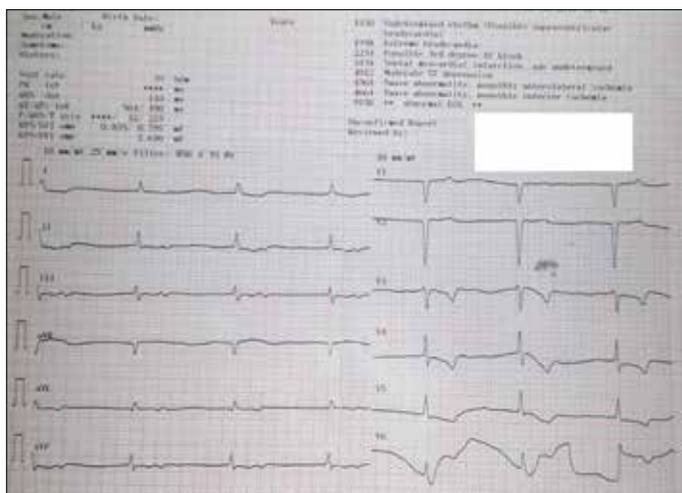


FIGURE 2. ECG showed junctional bradycardia

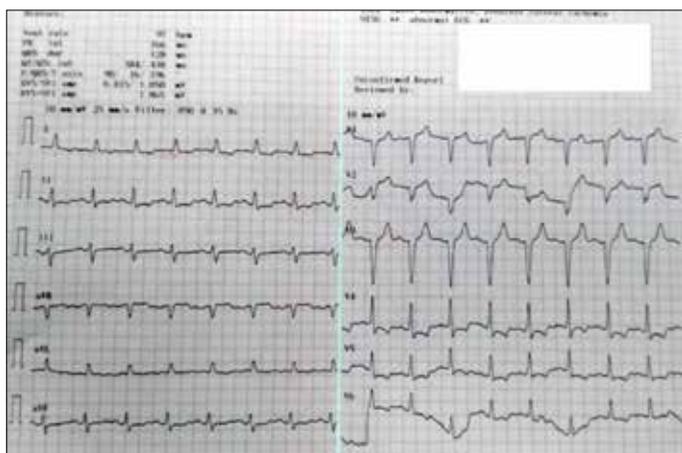


FIGURE 3. ECG showed a normal sinus rhythm after interventions

was 7.27, pCO₂ was 38.6 mmHg, pO₂ was 69 mmHg, HCO₃ was 17.7 mmol/L, base excess was -8, and oxyhemoglobin rate was 87.5%. No abnormalities were detected on initial brain computed tomography

(CT). An initial electrocardiogram (ECG) revealed sinus rhythm with a heart rate of 62 beats/min (Figure 1). After neurology consultation, 1000 mg phenytoin (loading dose of 15 mg/kg) in 250 mL of saline was intravenously infused over 45 min (infusion rate was in 22.2 mg/min and the concentration of phenytoin was 4 mg/mL).

Immediately after phenytoin infusion, ECG showed junctional bradycardia with a heart rate of 39 beats/min (Figure 2). The patient became unresponsive, and hypotension developed (blood pressure of 93/51 mmHg). Atropine (0.5 mg IV push) was administered immediately and repeated two times. Because of continued bradycardia and hypotension, transcutaneous pacing was initiated. Dopamine infusion was concurrently started at 10 µg/kg/min. The patient subsequently improved hemodynamically and neurologically, resulting in discontinuation of dopamine infusion and transcutaneous pacing. Fifteen minutes after the intervention, his ECG showed a normal sinus rhythm with a heart rate of 97 beats/min (Figure 3). The patient was admitted to the neurological intensive care unit.

Discussion

In this case, we present an example of a patient with phenytoin cardiotoxicity resulting in junctional bradycardia. This case is important because it shows that phenytoin can cause toxicity even though it is administered at the recommended dose and at a low infusion rate.

Phenytoin is an effective anticonvulsant that is used for partial and tonic-clonic seizures. Because phenytoin is used in the oral and parenteral form and it can rapidly reach emergency treatment levels, it is used as a first-line drug therapy for managing seizures in the emergency department. The main side effects of phenytoin are gingival hyperplasia, hirsutism, acne, and facial coarsening (3).

Two variables may be responsible for phenytoin toxicity: total dose and the rate of administration. Recommendations for phenytoin administration are shown Table 1 (1). In a review article, administering phenytoin at a slow rate (25 mg/min) for status epilepticus is recommended in geriatric patients and patients with known cardiovascular disease (4). In our patient, we infused phenytoin at a rate of 22.2 mg/min and the total dose was 15 mg/kg.

Phenytoin binds to the plasma protein at a high level (approximately 90%), and the free part is responsible for the pharmacological effects. Therefore, unbound serum phenytoin is high in patients with hypoalbumin or end-stage renal disease (5). Several equations have been developed for calculating free phenytoin concentration, and only albumin and total phenytoin concentrations were correlated with the free phenytoin concentration (6). Our patient had end-stage renal disease for which she was on hemodialysis. In our hospital's medical records, we found that our patient had a low albumin level (<3.4 g/dL) for the past 2 years. However, we did not measure the patient's albumin level on admission.

Propylene glycol is a commonly used solvent in various intravenous drug preparations, and it can also produce toxicity. Propylene glycol toxicity causes high anion gap metabolic acidosis. However, propyl-

Table 1. Recommendations for phenytoin administration

IV solution	1. The concentration of phenytoin should be ≤ 6.7 mg/mL 2. Infusion rate at ≤ 40 mg/min 3. Infuse only through a free-flowing, well-positioned IV needle 4. Infuse via piggyback IV arrangement
The patient	1. Reduce total phenytoin dose for low-weight patients and those with known or suspected phenytoin level >0 2. Reduce phenytoin concentration and rate of infusion for patient with known cardiac disease, abnormal ECG, and those >60 years
Observation	1. Periodically observe vital signs and symptoms for all patient and use a cardiac monitor for older patients, those with known cardiac disease, and those with changes in the vital sign

ene glycol toxicity is more common with lorazepam infusion. Phenytoin infusion should also be considered (7).

Conclusions

Emergency physicians should monitor patients for possible arrhythmic effects of intravenous phenytoin therapy. Additionally, geriatric patients and patients with history of cardiac disease may have an increased cardiotoxicity risk with phenytoin administration even if the recommended dose and infusion rate in patients with end-stage renal disease.

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